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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,736	01/06/2006	Catherine A Phillips	VET-1030-US	2610

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
10/21/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DOCKETING@BIOTECHNOLOGYLAWGROUP.COM

Office Action Summary	Application No.	Applicant(s)	
	10/530,736	PHILLIPS ET AL.	
	Examiner	Art Unit	
	MARIANNE DIBRINO	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,9-16 and 19-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,9-16,19-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response filed 6/28/09 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election [with traverse] of the species of radio-labeling with indium-111 oxide and imaging is by radioimaging, intravenous administration, T lymphocytes comprising CD8+ lymphocytes and tumor mucin peptide in Applicant's response filed 8/14/09 is acknowledged. Applicant's election of the linear peptide GSTAPPAHGVTSAPDTRPAP and administering lymphocytes intravenously by administering a glycoconjugate that comprises administering asialooromucoid in a telephonic interview with Applicant's representative Daniel M. Chambers on 12/7/09 is acknowledged.

Claims 1-4, 6, 9-16 and 19-28 are presently being examined.

3. Applicant is reminded that for the purpose of prior art rejections, the filing date of the instant claims is deemed to be the filing date of PCT/US03/32602, *i.e.* 10/10/03, as the provisional application does not support the claimed limitations of the instant invention (*i.e.*, the provisional application does not provide support for peripheral blood mononuclear cells, for labeling antigen-specific T lymphocytes with a label that is detectable by imaging, determining distribution of labeled antigen-specific T lymphocytes by imaging, administering a glycoconjugate, or administering IL-2. The provisional application only provides support for lymphoid cells obtained from blood, indium oxide or another radiolabel, and imaging by a combination of SPECT and CT or MRI or alternately by PET.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-4, 6, 9-11, 14, 15, 16, 19-28 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips *et al* (J. Immunotherapy, 2002, 25(6): S34, IDS reference) in view of Wright *et al* (J. Immunotherapy, 2000, 23(1): 2-10, IDS reference) and WO 98/37095 A2 (of record).

Phillips *et al* teach *in vivo* administration of ^{111}Indium-labeled CTL preparations stimulated against tumor mucin peptide, including by intravenous or intraperitoneal administration, in order to detect the localization of the CTL preparations to tumors or metastases. Phillips *et al* further teach serial CT and SPECT scans and that the

radiolabeled CTL preparations localized to tumors and to areas not previously identified as tumor metastases. Phillips *et al* teach comparison of data from two or more separate scans and fusion of such into a single display image.

Phillips *et al* do not explicitly teach the sequence of the tumor mucin peptide used for stimulation, nor explicitly teach that the CTL were stimulated against SEQ ID NO: 2 recited in instant claim 19. Phillips *et al* do not explicitly teach the protocol used for stimulating CTL that is recited in the instant claims.

WO 98/37095 A2 teaches that the 20-mer tandem repeat unit of MUC1 is the immunogenic fragment of MUC1 tumor associated antigen (*i.e.,* GSTAPPAHGVTSAPDTRPAP, see especially abstract and page 2 at lines 5-8).

Wright *et al* teach stimulating CTL in PBMC samples from humans with adenocarcinomas with Muc1 or mucin peptides and IL-2, and that the mucin epitope can bind and activate the TCR in the absence of antigen processing and MHC presentation (especially summary paragraph and paragraphs 3-4 of the introduction section).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have stimulated the CTL taught by Phillips *et al* as per the protocol taught by Wright *et al* using IL-2 and autologous PBMC and the immunogenic 20-mer tandom repeat unit of MUC 1 (*i.e.,* GSTAPPAHGVTSAPDTRPAP) and used the stimulated CTL in the detection/imaging method taught by Phillips *et al.*

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to detect and image tumors and their metastases.

Although Phillips *et al* do not explicitly teach that the imaging comprises a total body scan, Phillips *et al* teach looking at the biodistribution of the administered CTL over time. Therefore the claimed method appears to be the similar to the method of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show an unobvious distinction between the method of the instant invention and that of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Applicant has argued in the amendment and response filed 6/28/10 on pages 8-9, that the Philips et al abstract was not available until after 10 October 2002, the filing date [of] provisional application serial no. 60/417,303. However, Applicant is reminded that the priority date of the instant claims for the purpose of prior art rejections is the filing date of PCT/US03/32602, *i.e.,* 10 October 2003.

6. Claims 12-14 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips *et al* (J. Immunotherapy, 2002, 25(6): S34, IDS reference) in view of Wright *et al* (J. Immunotherapy, 2000, 23(1): 2-10, IDS reference) as applied to claims 1-4, 6, 9-11, 15, 16, 19-28 above, and further in view of Mukherji *et al* (Nucl. Med. Biol. 1988, 15(4): 419-427, IDS reference), WO 03/077864 A2 (9/25/03, IDS reference) and Ting *et al* (J. Immunol. 1986, 137(7): 2100-2106, of record).

Phillips *et al* and Wright *et al* have been discussed supra, hereafter referred to as "the combined references".

The combined references do not teach wherein the administering step comprises administering a glycoconjugate such as those recited in instant claims 12 and 13.

Mukherji *et al* teaches IL-2 and tumor antigen-stimulated cytotoxic lymphocytes from PBMC of metastatic cancer patients, labeling of said lymphocytes with Indium-111 and reinfusion of said lymphocytes, followed by study of biodistribution using a gamma camera at various time intervals. Mukherji *et al* further teach that the considerable degree of trapping of cells in the liver and spleen suggests that methods for reducing trapping by hepatosplenic cells need to be explored to maximize delivery of administered cells to appropriate tumor sites (see entire reference, especially abstract).

WO 03/077864 A2 teach that hyposialylated and desialylated proteins/glycoconjugates (also called asialoglycoconjugates) and cells which bear similar determinants are bound or trapped in the liver as a consequence of binding to the hepatic asialoglyoprotein receptors. WO 03/077864 A2 teaches that occupation of the receptor by the asialoglycoconjugate inhibits sequestration of the cells bearing similar determinants of interest in the liver and prevent infused cells from concentrating in the alveolar vasculature. WO 03/077864 A2 teaches that the glycoconjugates may be used to traffic or target cells in the body. WO 03/077864 A2 teaches that asialoglycoconjugates are able to bind to the hepatic parenchyma and Kupffer cell asialoglycoprotein receptors and keeps these receptors from binding and trapping cells bearing asialodeterminants. WO 03/077864 A2 teaches that parenteral, such as IV, administration of a glycoconjugate such as asialoorosomucoid may be used to block the hepatic asialoglycoprotein receptor and allow the cells bearing surface asialodeterminants to continue to circulate. WO 03/077864 A2 also teaches administering orosomucoid (AAG) for allowing the cell to circulate (especially Introduction, page 12 at the third full paragraph, paragraph spanning pages 12-13, claims, Figure 1).

Ting *et al* teach that CTL express asialo GM1 (AsGM1), *i.e.*, express a desialylated determinant (see entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered asialoorosomucoid or orosomucoid that is

taught by WO 03/077864 A2 in tandem or prior to administration of the indium-111-labeled CTL in the method of the combined references.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have reduced non-specific sequestration of the infused CTL as taught by Mukherji *et al* in the method taught by the combined references, particularly in light of the teaching of WO 03/077864 A2 that such administration reduces sequestration of cells bearing hyposialylated and desialylated determinants and the teaching of Ting *et al* that the CTL express such a determinant.

Applicant has argued in the amendment and response filed 6/28/10 on pages 8-9, that the Philips *et al* abstract was not available until after 10 October 2002, the filing date [of] provisional application serial no. 60/417,303. However, Applicant's argument has been fully considered but is not persuasive. Applicant is reminded that the priority date of the instant claims for the purpose of prior art rejections is the filing date of PCT/US03/32602, *i.e.,* 10 October 2003, and thus, the Philips *et al* abstract is available as prior art.

7. No claim is allowed.

8. Applicant is reminded that Applicant and the assignee of this application are required under 37 CFR 1.105 to provide the following information that the Examiner has determined is reasonably necessary to the examination of this application.

Applicant has provided the following abstract in Applicant's IDS filed 4/19/07:

J. Immunotherapy, 2002, 25(6): S34, Phillips *et al.* Phillips *et al* lists Inventor Phillips as well as Inventor Wright as authors of the abstract.

In the said abstract, the authors teach *in vivo* administration of ^{111}Indium-labeled CTL preparations stimulated against tumor mucin peptide, including by intravenous or intraperitoneal administration, in order to detect the localization of the CTL preparations to tumors or metastases.

In the biological sciences, it is customary for scientists to present their work to others at meetings, in the form of a poster presentation and/or in the form of an oral presentation with audio-visual materials. As such, the poster or oral presentation presented at the meeting comprises more data than is contained in an abstract.

In order to comply with the request for information under 37 C.F.R. 1.105, Applicant is requested to provide:

1. A copy of a poster if there was one presented; and
2. A statement describing all of the data that was presented on the poster or in an oral presentation, and how that data is related to the data of the instant specification. In addition, Applicant is requested to provide the sequence of the tumor mucin peptide, the conditions under which the CTL preparations were stimulated and what the source of the stimulating cells was, what conditions and other substances were used when administering the stimulated/labeled CTL, and whether or not total body scans were used in imaging.

In response to this request, Applicant is also requested to furnish: a statement describing additional presentations and/or abstracts presented by Applicants at scientific meetings wherein data pertinent to the subject matter was disclosed, and the contents of such disclosures, if such disclosures in fact occurred.

Note that compliance with the above requests cannot reasonably be considered burdensome since the Inventors were either present at, or aware of, any disclosures of the instant claimed subject mater at scientific meetings and events prior to the filing of the instant application.

The fee and certification requirements of 37 CFR 1.97 are waived for those documents submitted in reply to this requirement. This waiver extends only to those documents within the scope of this requirement under 37 CFR 1.105 that are included in the Applicant's first complete communication responding to this requirement. Any supplemental replies subsequent to the first communication responding to this requirement and any information disclosures beyond the scope of this requirement under 37 CFR 1.105 are subject to the fee and certification requirements of 37 CFR 1.97.

Applicant is reminded that the reply to this requirement must be made with candor and good faith under 37 CFR 1.56. Where Applicant does not have or cannot readily obtain an item of required information, a statement that the item is unknown or cannot be readily obtained may be accepted as a complete reply to the requirement for that item.

This requirement is an attachment of the enclosed Office action. A complete reply to the enclosed Office action must include a complete reply to this requirement. The time period for reply to this requirement coincides with the time period for reply to the enclosed Office action.

Applicant has argued in the amendment and response filed 6/28/10 on pages 8-9, that the Philips *et al* abstract was not available until after 10 October 2002, the filing date [of] provisional application serial no. 60/417,303. However, Applicant is reminded that the priority date of the instant claims for the purpose of prior art rejections is the filing date of PCT/US03/32602, *i.e.,* 10 October 2003. Applicant has not therefore complied with said request.

10. Applicant's amendment necessitated the new ground(s) of objection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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